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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	
Cheng LI and Mir IMRAN	Group Art Unit: 1654
Application No.: 10/664,697	Examiner: Anish Gupta
Filed: September 16, 2003	Confirmation No.: 5503
For: MULTIPLE-ARM PEPTIDE COMPOUNDS, METHODS OF MANUFACTURE AND USE IN THERAPY	

APPEAL BRIEF

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APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

A Notice of Appeal was filed on June 23, 2009 in connection with this application, and this paper was received in the U.S. Patent and Trademark Office on June 29, 2009. Accordingly, this Appeal Brief is timely filed on December 29, 2009 together with a four-month Petition for Extension of Time.

I. Real Party In Interest

The real party in interest in this application is Mir Imran.

II. Related Appeals and Interferences

None.

III. Status of Claims

Claims 1-4, 7-9, 14-17, 23, 24 and 26 are cancelled.

Claims 5, 6, 10-13, 18-22, 25 and 27-33 are rejected and are the subject of this appeal.

IV. Status of Amendments

No amendments after final rejection have been filed.

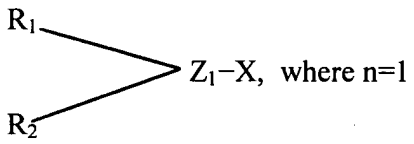
V. Summary of Claimed Subject Matter

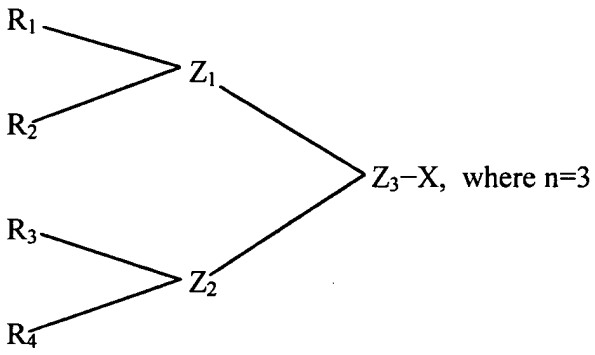
The present invention concerns peptide or protein molecules having multiple arms which contain specific sequences, domains or group which are useful to produce improved cell adhesion, proliferation, migration and spreading, anti-inflammation, healing response, antithrombogenic effect and the like. (Specification at page 1, lines 7-11). Thus,

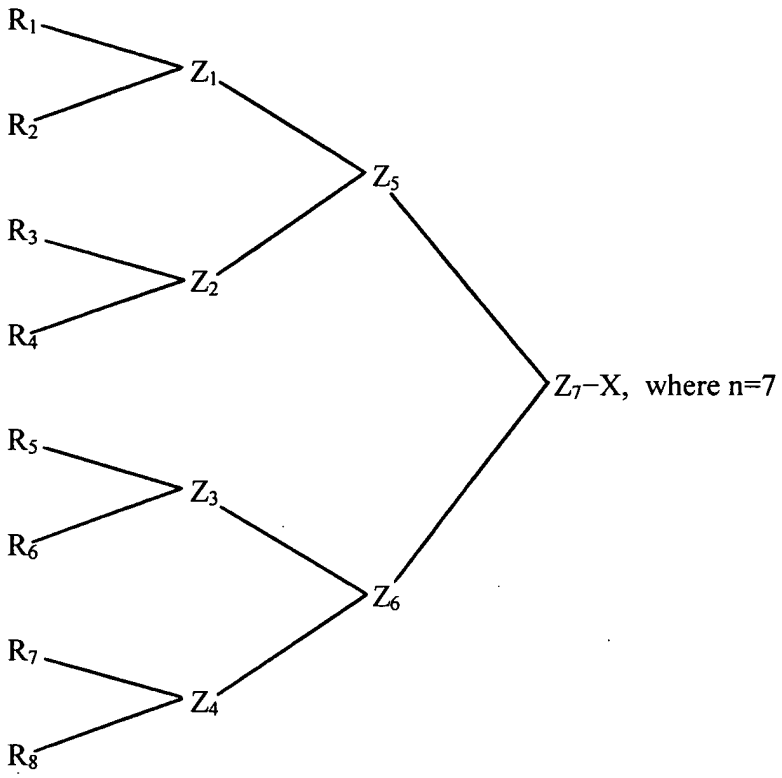
independent claim 5 recites a composition of matter for the active structure MAP-S wherein MAP is an organic molecule which is covalently bound to a substrate S. (Specification at page 9, lines 9-1). S is selected from the group consisting of metal, alloy, ceramic, natural polymer, synthetic polymer, bioabsorbable polymer, liquid polymer and combinations and blends thereof. (Specification at page 9, lines 12-14). See the Specification at page 9, line 14 to page 10, line 50, which describes that the organic structure MAP is selected from:

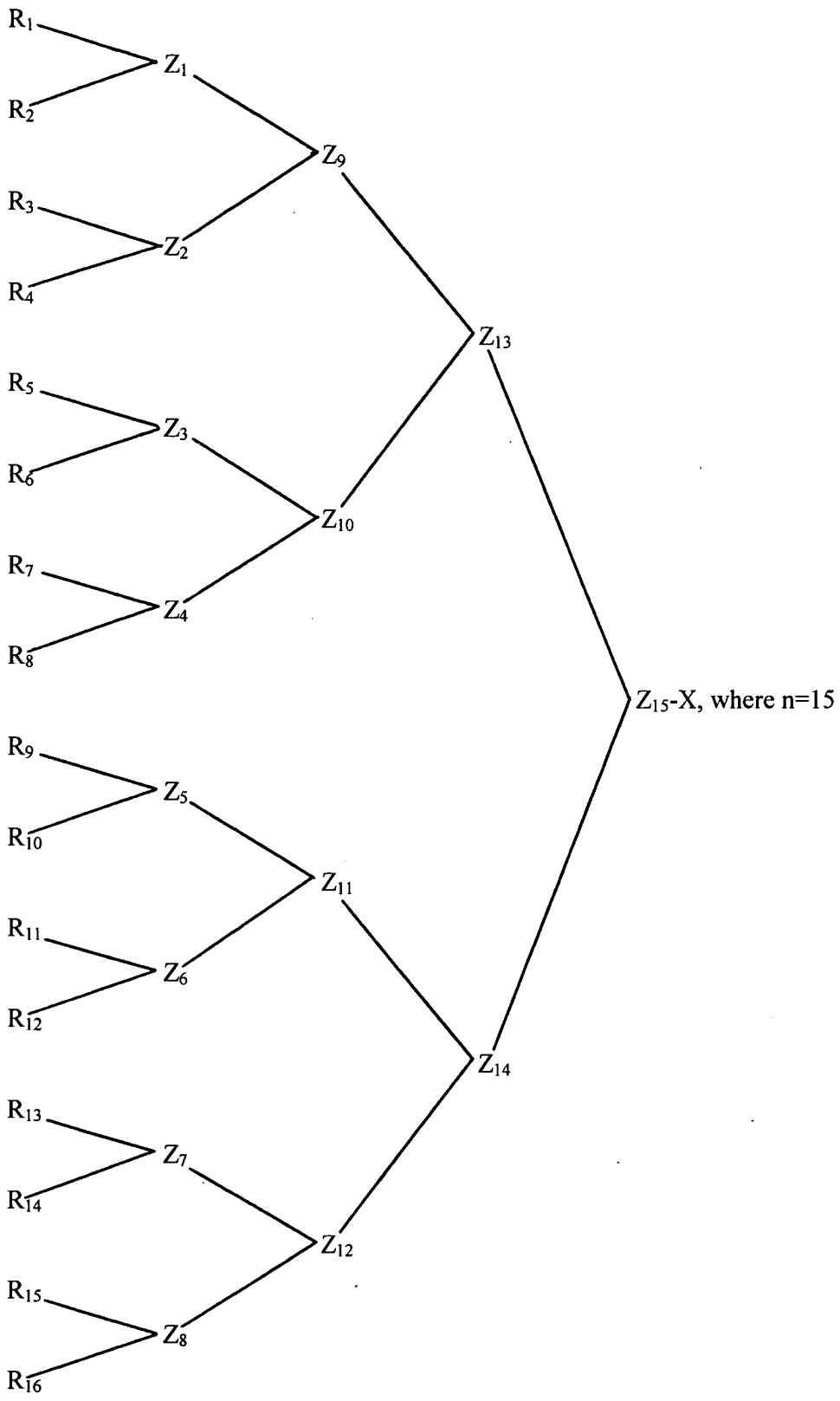
$(R)_{n+1}$-$(Z)_n$-X-

wherein n is selected from 1, 3, 7 or 15, producing the following structures:






R1
R2
Z1
R3
R4
Z2
Z5
R5
R6
Z3
R7
R8
Z4
Z6
Z7=X, where n=7



Each R contains any type and number of cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, adhesive or adhesion

barrier structures, and their combinations, with the proviso that, the MAP has active functional groups to covalently link the MAP structure to the surface of the substrate (S), located on group X, Z or R. Specification at page 11, lines 1-7). In addition, each R when present in the MAP structure comprises a total of up to about 100 amino acids (Specification at page 20, line 17 to page 21, line 2), and wherein each R_1 to R_{16} comprises GTPGPQGIAGQRGVV (SEQ ID NO:1)(Specification at page 11, lines 15-17; page 21, line 16 to page 22, line 4; page 22, line 19 to page 23, line 5; page 24, lines 2-5; page 25, lines 2-5; and page 26, lines 2-5).

X is an active or protected linking group selected from the group consisting of amine, linked amino acids of 1 to 5 in length, (X1 to X5) which when present are the same or different, carboxylic acid, anhydride, hydroxyl, carbonyl succinimide (NHS) and siloxane. (Specification at page 11, lines 8-11; and original claim1 at page 83, lines 8-11).

Each Z is independently selected from lysine or ornithine. (Specification at page 11, lines 12-13).

VI. Grounds of Rejection to be Reviewed on Appeal

1. Whether claims 5, 6, 10-13, 18-22, 25 and 27-33 are unpatentable under 35 U.S.C. 103(a) over Dang et al. (U.S. Patent Publication No. 2003/0113478) in view of Tam ("Synthesis and Applications of Branched Peptides and Immunological Methods and Vaccines" in Peptides: Synthesis, Structures and Applications, B. Gutte, (ed), Academic Press, San Diego, CA, pages 455-500, (1995)).
2. Whether claims 5, 10-13, 18-22 and 25 are unpatentable under 35 U.S.C. 103(a) over Bhatnagar (WO 91/02537) in view of Tam ("Synthesis and Applications of Branched Peptides and Immunological Methods and Vaccines" in Peptides: Synthesis, Structures and Applications, B. Gutte, (ed), Academic Press, San Diego, CA, pages 455-500, (1995)).

VII. Argument

1. Rejection Under 35 USC 103(a) over Dang et al. in view of Tam

Claims 5, 6, 10-13, 18-22, 25 and 27-33 were rejected under 35 U.S.C. §103 as being unpatentable over Dang et al. in view of Tam. For at least the reasons set forth below, reversal of this rejection is respectfully requested.

Independent claim 5 recites a composition of matter for the active structure MAP-S. MAP is an organic molecule covalently bound to a substrate S. MAP has the general structure $(R)_{n+1}$-$(Z)_n$-X- , wherein X is a linking group, Z is lysine or ornithine, and each R when present in the MAP structure comprises a total of up to about 100 amino acids, and wherein each R_1 to R_{16} comprises GTPGPQGIAGQRGVV (SEQ ID NO:1). The R moiety may contain cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, or adhesive or adhesion barrier structures.

Dang et al. is purported to describe covalently coating a ePTFE graft material with the peptide GTPGPQGIAGQRGVV. This coated material appeared to promote the migration and proliferation of healthy endothelial cells.

Dang et al. does not describe or suggest the use of a MAP structure to allow covalent attachment of the peptide GTPGPQGIAGQRGVV to a substrate. However, the Examiner has asserted that it would have been obvious to use a MAP structure in the coated materials of Dang et al. in view of Tam. In particular, the Examiner asserts that Tam "states, ***as inhibitors***, branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact" (emphasis added, Office Action of December 23, 2008 at page 4, lines 14-16). The Examiner concludes, therefore, that "[i]t would have been obvious to one of ordinary skill in the art to incorporate the peptide GTPGPQGIAGQRGVV into a multimeric peptide structure (MAP) because branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact and MAPs have increased binding to cell surfaces, relative to the monomer" (Office Action of December 23, 2008 at page 4, line 20 to page 5, line 1).

Neither Dang et al. nor Tam, either alone or in combination, would have suggested each and every element of the claimed subject matter. The Examiner has failed to provide articulated reasoning based on a rational underpinning to support the legal conclusion of obviousness. (See MPEP 2143.01, paragraph IV (citing *KSR International Co. V. Teleflex Inc.*, 550 U.S. 398 (citations omitted)).) Furthermore, in addition to the aforementioned deficiencies of Dang et al., Tam et al. teaches away from any relevant modification of this document.

As discussed above, the MAP-S structures recited by the present claims function as cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, or adhesive or adhesion barrier structures. That is, they act as agonists to

promote the function that the peptide GTPGPQGIAGQRGVV would normally have as presented *in vivo*.

Tam, on the other hand, describes procedures for making branched peptides for use in immunological methods and vaccines. Tam explains on page 461 (under the heading "A. Definition and Classification of Peptide Antigens") that the selection of peptide sequences as immunogens in branched peptides relies on two criteria: immunogenicity and antigenicity. Immunogenicity is defined as "the ability of a peptide to elicit high-titered antibody", while "antigenicity provides the ability of the antibody to recognize the protein from which it is derived and is governed by the conformation or the shape of the peptide." Tam states that "the portion or portions of the peptide or protein responsible to provide the "shape" of the antigen is operationally defined as a B-cell epitope while the portion responsible for inducing the antibody production is operationally defined as a T-cell epitope." Thus, Tam regards immunogenicity and antigenicity as necessary for producing the branched peptides described therein and draws a distinction between these two criteria.

Tam provides MAP-peptide inhibitor structures and not MAP-peptide agonists

Nowhere, however, does Tam indicate that it is necessary to retain the biological activity of the peptides or proteins used to make branched peptides. Accordingly, Tam could not have possibly guided one of skill in the art to the claimed subject matter, which recites that the R portion of the MAP-S structure "contains any type and number of cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, adhesive or adhesion barrier structures, and their combinations."

Moreover, Tam teaches away from the claimed subject matter. Tam teaches that including a peptide in a MAP structure produces ***an inhibitor*** due to branched peptides with clustered positive charges (Tam at page 476). Thus, from the teachings of Tam, one would expect that including GTPGPQGIAGQRGVV in a MAP structure would produce an inhibitor rather than the agonists recited by the present claims. Clearly, the applied art would not have guided one to the claimed subject matter. A prior art reference must be considered in its entirety including portions that would lead away from the claimed invention. See *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); *KSR International Co. V. Teleflex Inc.*, 550 U.S. 398; and MPEP 2141.02, paragraph VI.

As explained above, when considered in its entirety, Tam does indeed teach away from the claimed subject matter. Obviousness cannot be established where the references

teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983); See also *United States v. Adams*, 383 U.S. 39, 40 (1966) and *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 416 (2007) (citing the Adams court).

On page 5, lines 1-6, of the Office Action of December 23, 2008, the Examiner states that:

> "Note the primary reference disclose that the peptide promoted the migration and proliferation of healthy endothelial cells. There would have been a reasonable expectation of success because MAP branched peptides have been shown to have increased binding of to cell surfaces. Tam teaches that the Clustering, which allows for stronger binding than their monomers by allowing multiple points of contact could be achieved by adsorption on a surface or by coupling to a carrier or sepharose bead."

Thus, the Examiner has totally disregarded Tam's teaching away from the claimed subject matter. That is, the Examiner notes that Dang et al. purportedly describe the GTPGPQGIAGQRGVV peptide promoting the migration and proliferation of endothelial cells. But then the Examiner makes no mention whatsoever that Tam teaches that including such peptides on a MAP structure would be expected to produce an inhibitor of that peptide's agonist activity. There simply would not have been "a reasonable expectation of success", as asserted by the Examiner, because the very reference being relying on (i.e., Tam) indicates that no agonist activity in the MAP bound peptide would be expected.

The convoluted reasoning of the Examiner continues on page 7 of the Office Action of December 23, 2008. There, it is stated that:

> "However the teaching of Tam is applicable to not only inhibitors but also other biological peptides. While the reference states that here is increased binding of branched peptides to proteins or cell surfaces compared that of native protein has been exploited for applications as inhibitors. However, this would not lead one to conclude that MAP peptides can only be utilized in inhibitors. Rather, reading the reference, one would be lead to believe that increased binding of branched peptides to proteins or cell surfaces compared that of native protein would be observed in all peptides not only inhibitors."

Tam provides no basis for the Examiner's conclusion that "one would be lead to believe that increased binding of branched peptides to proteins or cell surfaces compared that of native protein would be observed in all peptides not only inhibitors." That is, the description on page 476 of Tam appears to be a general phenomenon observed with MAP peptides, i.e., binding peptides to MAP structures leads to clustered positive charges which can lead to stronger binding than in the monomer peptides. It has been observed in some cases that the binding is strong enough to produce an inhibitor molecule. From the description in Tam, these MAP structures would also be expected to have increased immunogenicity and antigenicity. Tam has not described a single instance of a peptide which retains biological activity once the peptide is included in a MAP structure. The Examiner's statement otherwise is purely conjecture. The uses discussed by the Examiner, such as immunoassays, serodiagnosis, epitope mapping and affinity purification, are all uses which rely on the antigenicity of the MAP peptides. No discussion of retention of biological activity of the peptides in the MAP structures for such uses has been described by Tam. Consequently, there can be no reasonable expectation of success based on the combination of references urged by the Examiner. Obviousness cannot be established where there is no expectation of success based on the combination or modification of references. *KSR International Co. V. Teleflex Inc.*, 550 U.S. 398. See also MPEP 2143.02.

For at least the above reasons, reversal of the rejection based on 35 U.S.C. §103 over Dang et al. in view of Tam is respectfully requested.

2. Rejection Under 35 USC 103(a) over Bhatnagar in view of Tam

Claims 5, 10-13, 18-22 and 25 were rejected under 35 U.S.C. §103 as being unpatentable over Bhatnagar in view of Tam. For at least the reasons set forth below, reversal of this rejection is respectfully requested.

Independent claim 5 recites a composition of matter for the active structure MAP-S. MAP is an organic molecule covalently bound to a substrate S. MAP has the general structure $(R)_{n+1}$-$(Z)_n$-X- , wherein X is a linking group, Z is lysine or ornithine, and each R when present in the MAP structure comprises a total of up to about 100 amino acids, and wherein each R_1 to R_{16} comprises GTPGPQGIAGQRGVV (SEQ ID NO:1). The R moiety may contain cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, or adhesive or adhesion barrier structures.

Bhatnagar is purported to describe the covalent attachment of the peptide GTPGPQGIAGQRGVV to a substrate. Bhatnagar indicates that there may be enhanced binding of vertebrate cells to such a coated substrate.

Bhatnagar does not describe or suggest the use of a MAP structure to allow covalent attachment of the peptide GTPGPQGIAGQRGVV to a substrate. However, the Examiner has asserted that it would have been obvious to use a MAP structure in the coated materials of Bhatnagar in view of Tam. In particular, the Examiner asserts that Tam "states, ***as inhibitors***, branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact" (emphasis added, Office Action of December 23, 2008 at page 6, lines 4-6). The Examiner concludes, therefore, that "[i]t would have been obvious to one of ordinary skill in the art to incorporate the peptide GTPGPQGIAGQRGVV into a multimeric peptide structure (MAP) because branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact and MAPs have increased binding to cell surfaces, relative to the monomer" (Office Action of December 23, 2008 at page 6, lines 10-14).

Neither Bhatnagar nor Tam, either alone or in combination, would have suggested each and every element of the claimed subject matter. The Examiner has failed to provide articulated reasoning based on a rational underpinning to support the legal conclusion of obviousness. (See MPEP 2143.01, paragraph IV (citing *KSR International Co. V. Teleflex Inc.*, 550 U.S. 398 (citations omitted)).) Furthermore, in addition to the aforementioned deficiencies of Bhatnagar, Tam et al. teaches away from any relevant modification of this document.

As discussed above, the MAP-S structures recited by the present claims function as cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, or adhesive or adhesion barrier structures. That is, they act as agonists to promote the function that the peptide GTPGPQGIAGQRGVV would normally have as presented *in vivo*.

Tam, on the other hand, describes procedures for making branched peptides for use in immunological methods and vaccines. Tam explains on page 461 (under the heading "A. Definition and Classification of Peptide Antigens") that the selection of peptide sequences as immunogens in branched peptides relies on two criteria: immunogenicity and antigenicity. Immunogenicity is defined as "the ability of a peptide to elicit high-titered antibody", while "antigenicity provides the ability of the antibody to recognize the protein from which it is derived and is governed by the conformation or the shape of the peptide." Tam states that

"the portion or portions of the peptide or protein responsible to provide the "shape" of the antigen is operationally defined as a B-cell epitope while the portion responsible for inducing the antibody production is operationally defined as a T-cell epitope." Thus, Tam regards immunogenicity and antigenicity as necessary for producing the branched peptides described therein and draws a distinction between these two criteria.

Tam provides MAP-peptide inhibitor structures and not MAP-peptide agonists

Nowhere, however, does Tam indicate that it is necessary to retain the biological activity of the peptides or proteins used to make branched peptides. Accordingly, Tam could not have possibly guided one of skill in the art to the claimed subject matter, which recites that the R portion of the MAP-S structure "contains any type and number of cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, adhesive or adhesion barrier structures, and their combinations."

Moreover, Tam teaches away from the claimed subject matter. Tam teaches that including a peptide in a MAP structure produces ***an inhibitor*** due to branched peptides with clustered positive charges (Tam at page 476). Thus, from the teachings of Tam, one would expect that including GTPGPQGIAGQRGVV in a MAP structure would produce an inhibitor rather than the agonists recited by the present claims. Clearly, the applied art would not have guided one to the claimed subject matter. A prior art reference must be considered in its entirety including portions that would lead away from the claimed invention. See *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); *KSR International Co. V. Teleflex Inc.*, 550 U.S. 398; and MPEP 2141.02, paragraph VI.

As explained above, when considered in its entirety, Tam does indeed teach away from the claimed subject matter. Obviousness cannot be established where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983); See also *United States v. Adams*, 383 U.S. 39, 40 (1966) and *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 416 (2007) (citing the Adams court).

On page 6, lines 14-19, of the Office Action of December 23, 2008, the Examiner states that:

"Note the primary reference disclose that the peptide promoted the migration and proliferation of healthy endothelial cells. There would have been a reasonable expectation of success because MAP branched peptides have been shown to have increased binding of to cell surfaces. Tam teaches that the Clustering, which allows for stronger binding than their monomers by allowing multiple points of contact could be achieved by adsorption on a surface or by coupling to a carrier or sepharose bead."

Thus, the Examiner has totally disregarded Tam's teaching away from the claimed subject matter. That is, the Examiner notes that Bhatnagar purportedly describes the GTPGPQGIAGQRGVV peptide promoting the migration and proliferation of endothelial cells. But then the Examiner makes no mention whatsoever that Tam teaches that including such peptides on a MAP structure would be expected to produce an inhibitor of that peptide's agonist activity. There simply would not have been "a reasonable expectation of success", as asserted by the Examiner, because the very reference being relying on (i.e., Tam) indicates that no agonist activity in the MAP bound peptide would be expected.

The convoluted reasoning of the Examiner continues on page 7 of the Office Action of December 23, 2008. There, it is stated that:

"However the teaching of Tam is applicable to not only inhibitors but also other biological peptides. While the reference states that here is increased binding of branched peptides to proteins or cell surfaces compared that of native protein has been exploited for applications as inhibitors. However, this would not lead one to conclude that MAP peptides can only be utilized in inhibitors. Rather, reading the reference, one would be lead to believe that increased binding of branched peptides to proteins or cell surfaces compared that of native protein would be observed in all peptides not only inhibitors."

Tam provides no basis for the Examiner's conclusion that "one would be lead to believe that increased binding of branched peptides to proteins or cell surfaces compared that of native protein would be observed in all peptides not only inhibitors." That is, the description on page 476 of Tam appears to be a general phenomenon observed with MAP peptides, i.e., binding peptides to MAP structures leads to clustered positive charges which can lead to stronger binding than in the monomer peptides. It has been observed in some cases that the binding is strong enough to produce an inhibitor molecule. From the

description in Tam, these MAP structures would also be expected to have increased immunogenicity and antigenicity. Tam has not described a single instance of a peptide which retains biological activity once the peptide is included in a MAP structure. The Examiner's statement otherwise is purely conjecture. The uses discussed by the Examiner, such as immunoassays, serodiagnosis, epitope mapping and affinity purification, are all uses which rely on the antigenicity of the MAP peptides. No discussion of retention of biological activity of the peptides in the MAP structures for such uses has been described by Tam. Consequently, there can be no reasonable expectation of success based on the combination of references urged by the Examiner. Obviousness cannot be established where there is no expectation of success based on the combination or modification of references. *KSR International Co. V. Teleflex Inc.,* 550 U.S. 398. See also MPEP 2143.02.

For at least the above reasons, reversal of the rejection based on 35 U.S.C. §103 over Bhatnagar in view of Tam is respectfully requested.

CONCLUSION:

From the foregoing, reversal of all the rejections based on 35 U.S.C. §103 is believed to be in order.

Respectfully submitted,

BELL & ASSOCIATES

Date: December 29, 2009

By: 

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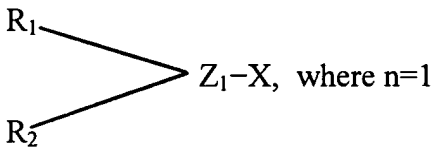
CLAIMS APPENDIX

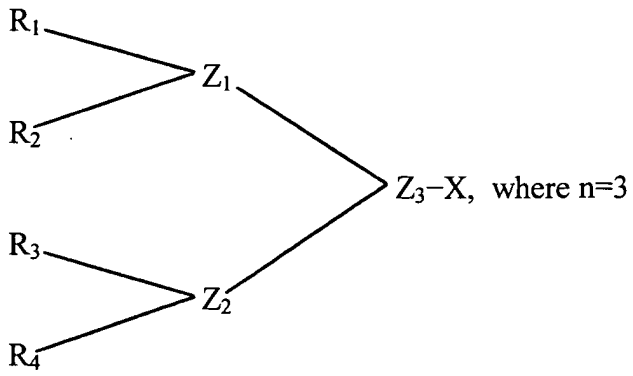
The claims on appeal are set forth below:

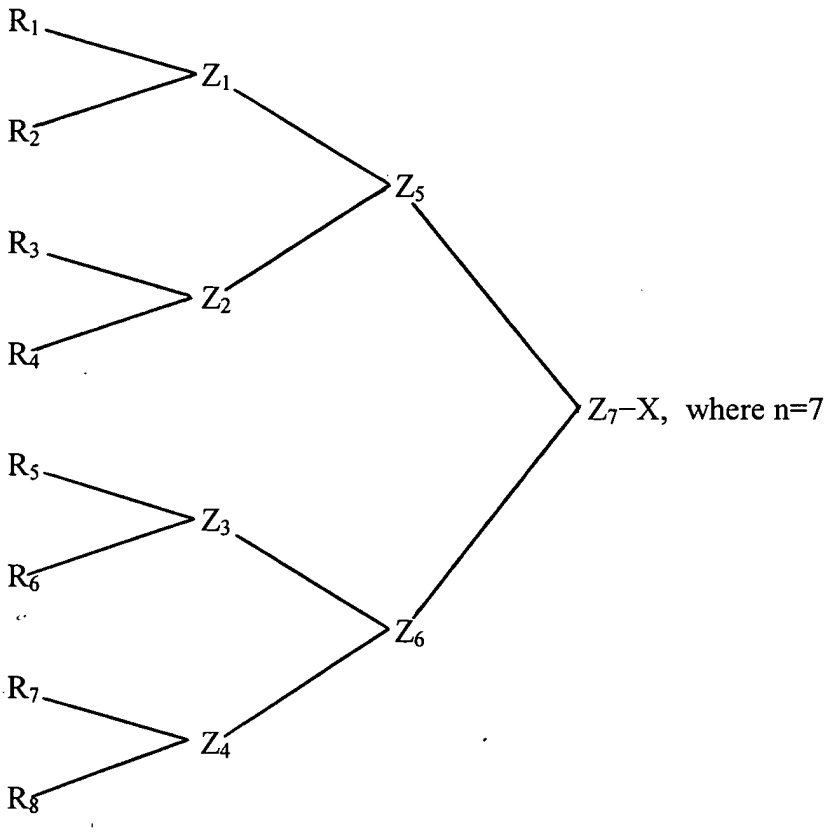
5. A composition of matter for the active structure MAP-S wherein MAP is an organic molecule which is covalently bound to a substrate S, wherein S is selected from the group consisting of metal, alloy, ceramic, natural polymer, synthetic polymer, bioabsorbable polymer, liquid polymer and combinations and blends thereof, and the organic structure MAP is selected from:

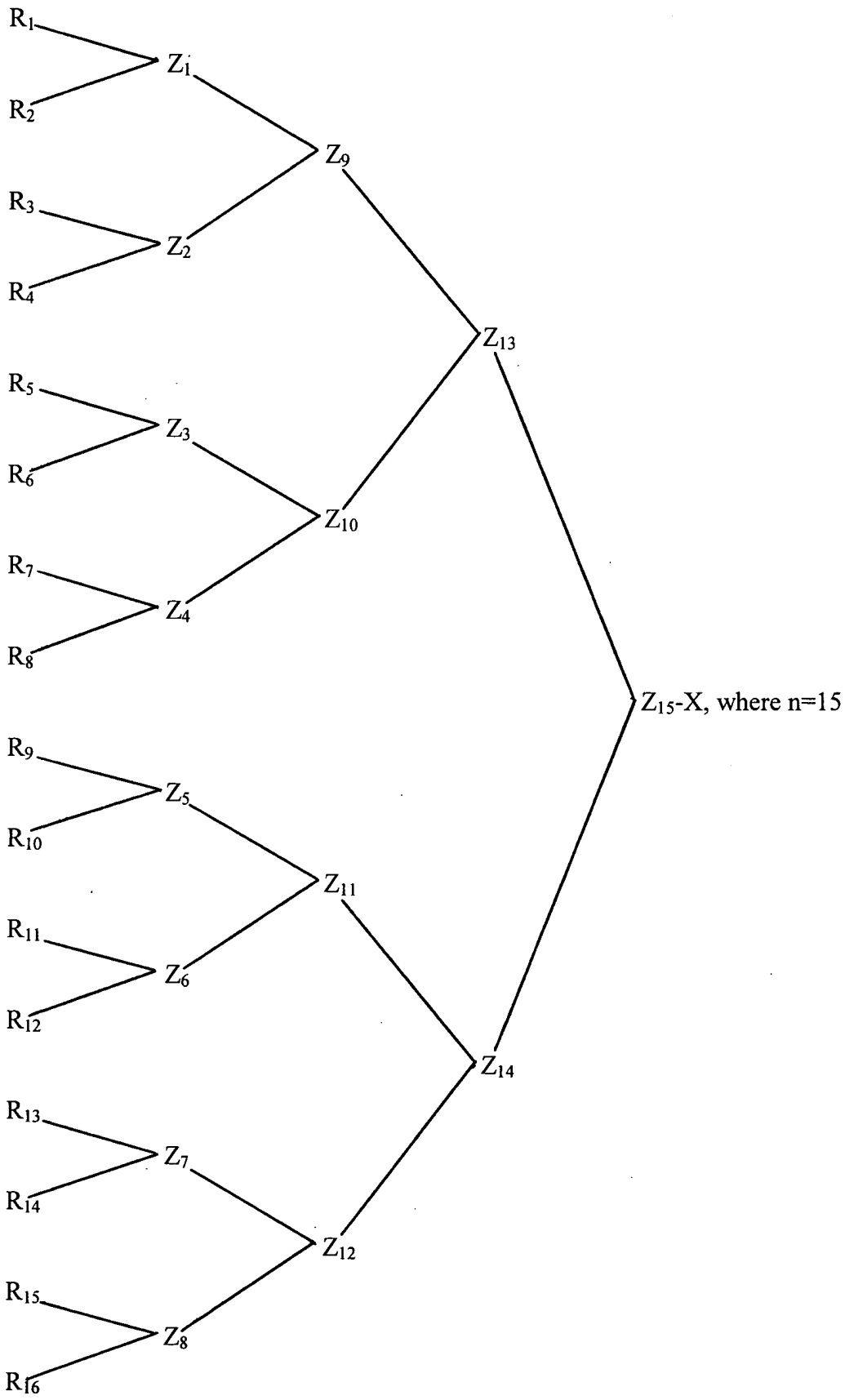
$(R)_{n+1}$-$(Z)_n$-X-

wherein n is selected from 1, 3, 7 or 15, producing the following structures:




R_1
R_2
R_3
R_4
Z_1
Z_2
Z_3–X, where n=3


R_1
R_2
R_3
R_4
R_5
R_6
R_7
R_8
Z_1
Z_2
Z_3
Z_4
Z_5
Z_6
Z_7–X, where n=7


R1
R2
Z1
R3
R4
Z2
Z9
R5
R6
Z3
R7
R8
Z4
Z10
Z13
R9
R10
Z5
R11
R12
Z6
Z11
R13
R14
Z7
R15
R16
Z8
Z12
Z14
Z15-X, where n=15

each R contains any type and number of cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, adhesive or adhesion barrier structures, and their combinations, with the proviso that, the MAP has active functional groups to covalently link the MAP structure to the surface of the substrate (S), located on group X, Z or R;

X is an active or protected linking group selected from the group consisting of amine, linked amino acids of 1 to 5 in length, (X1 to X5) which when present are the same or different, carboxylic acid, anhydride, hydroxyl, carbonyl succinimide (NHS) and siloxane;

each Z is independently selected from lysine or ornithine;

each R when present in the MAP structure comprises a total of up to about 100 amino acids, and wherein each R_1 to R_{16} comprises GTPGPQGIAGQRGVV (SEQ ID NO:1).

6. The composition of matter of Claim 5 wherein S is selected from the group consisting of hydroxylapatite, stainless steel, cobalt-chromium-molybdenum alloy, titanium, titanium alloy, polypropylene, polyethylene, polystyrene, polyether, polyamide/polyethylene copolymer, polychloroprene, polyester, polyvinyl chloride, polyolefin, polyphenolic, polyhydroxyacid, ABS epoxy, polytetrafluoroethylene, expanded polytetrafluoroethylene, polytetrafluoroethylene/polyethylene copolymer, fluorinated ethylene propylene, polyvinylidene, hexafluoropropylene, polyurethane, polysiloxane, polyisoprene, silicone, styrene butadiene, natural rubber, latex rubber, polyethyleneterephthalate, polycarbonate, polyamide, polyaramid, polyaryl ether ketone, polyacetal, polyphenylene oxide, polysulfone, polyethersulfone, regenerated cellulose, polyamino acids, polyarylsulfone, polyphenylene sulphide, polybutyl-terephthalate (PBT), poly(glycolide), HEMA and combinations thereof.

10. The composition of matter of Claim 5 wherein Z_1 to Z_{15} is lysine.

11. The composition of matter of Claim 5 wherein MAP is MAP4 and R_1 to R_4 are each independently selected from linear peptides having about 50 amino acids or less.

12. The composition of matter of Claim 5 wherein MAP is MAP8 and R_1 to R_8 are each independently selected from linear peptides having about 50 amino acids or less.

13. The composition of matter of Claim 5 wherein MAP is MAP16 and R_1 to R_{16} are each independently selected from linear peptides having about 50 amino acids or less.

18. The composition of matter of Claim 5 wherein

S is selected from the group consisting of polytetrafluoroethylene (PTFE) and hydroxylapatite;

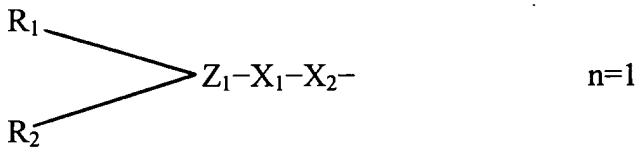
X is X_1-X_2, and X_1 and X_2 are selected from the group consisting of carboxyl and amino acid;

Z_1 to Z_{15} are lysine; and

R_1 to R_{16} are GTPGPQGIAGQRGVV (SEQ ID NO:1).

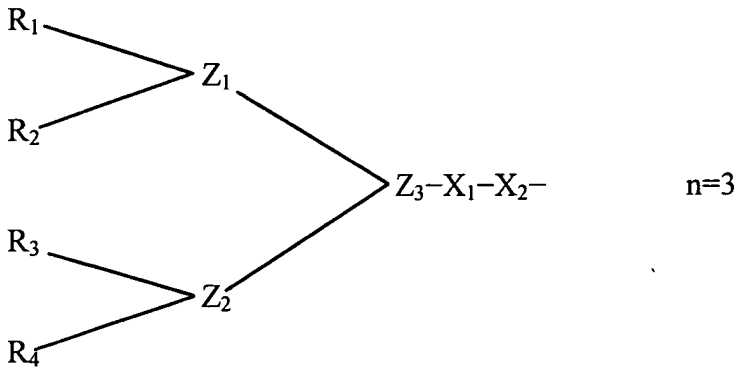
19. The composition of matter of Claim 5 wherein:

MAP is MAP2 of the structure:



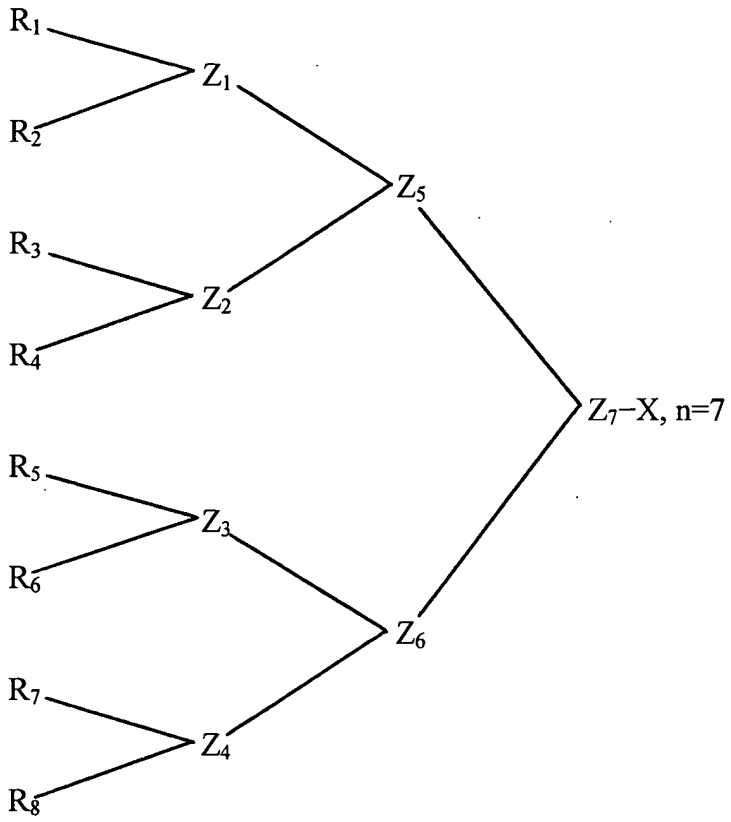
Z_1 is lysine and R_1 and R_2 are each GTPGPQGIAGQRGVV (SEQ ID NO:1);

MAP is MAP4 of the structure:



Z_1, Z_2 and Z_3 are lysine and R_1, R_2, R_3 and R_4 are each GTPGPQGIAGQRGVV (SEQ ID NO:1); or

MAP is MAP8 of the structure:



Z_1 to Z_7 are lysine and R_1 to R_8 are each GTPGPQGIAGQRGVV (SEQ ID NO:1); and X is $-X_1-$ or $-X_1-X_2-$ wherein X_1 and X_2 are selected from lysine, ornithine or alanine.

20. A pharmaceutical composition which comprises:

a pharmaceutically acceptable amount of MAP of Claim 5 in combination with a pharmaceutically acceptable carrier.

21. A pharmaceutical composition which comprises a pharmaceutically acceptable amount of MAP2, MAP4 or MAP8 of Claim 5 with a pharmaceutically acceptable carrier.

22. An implant comprising: a matrix formed of a multiple arm peptide-substrate (MAP-S) formed of a biomaterials coated substrate S and a multiple MAP peptide of Claim 5 combined by covalent binding to the substrate, wherein the MAP peptide has terminal ligands which have

enhanced properties for cell adhesion, migration, cell differentiation, cell proliferation, anti-inflammation, anti-thrombogenesis, cell growth, adhesion barrier and combinations thereof.

25. The implant of Claim 22 wherein the peptide MAP has a peptide sequence selected from the group consisting of MAP ID NO:13, MAP ID NO:14, MAP ID NO:15, MAP ID NO:22, MAP ID NO:23, MAP ID NO:24, MAP ID NO:31, MAP ID NO:32, MAP ID NO:33, MAP ID NO:40, MAP ID NO:41 and MAP ID NO:42.

27. The implant of Claim 30 wherein:

the peptide MAP is selected from a MAP4 or MAP8.

28. The implant of Claim 27 wherein:

R_1 to R_8 when present are GTPGPQGIAGQRGVV (SEQ ID NO:1), Z_1 to Z_7 are lysine, and X_1 and X_2 are selected from β-ala-COOH, β-ala-$CONH_2$, lys, or lys(NH_2).

29. The implant of Claim 28 wherein S is selected from the group consisting of e-PTFE, PTFE, polysulfone, polyurethane, silicone, titanium and titanium alloy.

30. The implant of Claim 25 wherein the substrate is selected from polymer materials selected from the group consisting of hydrocarbons, fluorocarbons, elastomers, engineering thermoplastics, and metallic materials.

31. The implant of Claim 30 wherein the hydrocarbon polymer material is selected from the group consisting of polypropylene, polyethylene, polystyrene, polyether, polyamide/polyethylene copolymer, polychloroprene, polyester, polyvinyl chloride, polyolefin, polyphenolic, polyhydroxyacid, ABS epoxy, and corresponding copolymers and blends; the fluorocarbon polymer material is selected from the group consisting of polytetrafluoroethylene, expanded polytetrafluoroethylene, polytetrafluoroethylene/polyethylene copolymer, fluorinated ethylene propylene, polyvinylidene fluoride, hexafluoropropylene, and corresponding copolymers and blends; the elastomer polymer material is selected from the group consisting of polyurethane, polysiloxane, polyisoprene, silicone, styrene butadiene, natural rubber, latex

rubber, and corresponding copolymers and blends; the engineering thermoplastic polymer material is selected from the group consisting of polyethyleneterephthalate, polycarbonate, polyamide, polyaramid, polyaryl ether ketone, polyacetal, polyphenylene oxide, polysulfone, polyethersulfone, regenerated cellulose, polyamino acids, polyarylsulfone, polyphenylene sulphide, polybutyl-terephthalate (PBT), poly(glycolide), HEMA and corresponding copolymers and blends; and the metallic material is selected form the group consisting of stainless steel, cobalt-chromium-molybdenum alloy, pure titanium, and titanium alloys.

32. The composition of matter of Claim 5 wherein each R when present in the MAP structure comprises a total of up to about 50 amino acids, and wherein each R_1 to R_{16} comprises GTPGPQGIAGQRGVV (SEQ ID NO:1).

33. The composition of matter of Claim 5 wherein each R when present in the MAP structure is GTPGPQGIAGQRGVV (SEQ ID NO:1).

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.